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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,729	11/13/2001	Moses Rodriguez	1199-1-005CIP2	4304

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EXAMINER

KOLKER, DANIEL E

ART UNIT PAPER NUMBER

1649

DATE MAILED: 05/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	10/010,729		RODRIGUEZ ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Daniel Kolker		1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 06 March 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 42,43,62,63,65,73 and 91-93 is/are pending in the application.
- 4a) Of the above claim(s) 62,63 and 65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 42,43,73 and 91-93 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 42,43,62,63,65,73 and 91-93 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Applicant's remarks and amendments filed 6 March 2006 have been entered. Claims 1 – 41, 44 – 61, 64, 66 – 72, and 74 – 90 are canceled. Claims 91 – 93 are new. Claims 42 – 43, 62 – 63, 65, 73, and 91 – 93 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Election/Restrictions***

3. Claims 62 – 63 and 65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 28 March 2005.

In the reply filed 28 March 2005, applicant elected the antibody sHIgM22 (LYM 22) for prosecution on the merits. This antibody binds to oligodendrocytes (specification, p. 127, and Figure 25, and p. 26, description of Figure 25) and comprises SEQ ID NO:7 and 9 as the heavy and light chain variable regions respectively (see specification, pp. 29 – 30, descriptions of Figures 35 and 36). Claim 62 as originally examined was confusing and the scope of the claim was unclear. Applicant's amendments to claim 62 now make it quite clear that the claim does not read on the elected invention, but rather on an anti-idiotypic antibody capable of binding to either SEQ ID NO:7 or SEQ ID NO:9. These are the regions of sHIgM22 responsible for recognizing the antigen, so an antibody produced by injecting either of these sequences into an immunocompetent host would bind to sHIgM22. As claim 62 and dependent claims 63 and 65 are clearly drawn to non-elected subject matter, the claims do not read on the elected invention and thus are withdrawn.

Applicant retains the right to have process claims which depend from elected product claims examined, subject to the conditions set forth on pp. 8 – 9 of the restriction requirement mailed 28 October 2004, should any product claim be found allowable.

4. This application contains claims 62 – 63 and 65 drawn to an invention nonelected with traverse the reply filed 28 March 2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
5. Claims 42 – 43, 73, and 91 – 93 are under examination.

***Withdrawn Rejections and Objections***

6. The following objections or rejections made in the previous office action are withdrawn:

A) The objection to claims 42 and 73 are withdrawn in light of the amendments.

B) The rejections under 35 USC § 101 are withdrawn; the claims now read on isolated antibodies and compositions, not on products of nature.

C) The rejection of claim 73 under 35 USC 112, first paragraph for failing to meet the enablement requirement because the hybridoma was not deposited is withdrawn. Claim 73 is now an independent claim and a skilled artisan could make the composition without access to the hybridoma.

D) The rejection of claim 73 under 35 USC 112, first paragraph for failing to provide adequate written description is withdrawn in light of the amendments.

***Rejections Maintained and Necessitated by Amendment***

***Priority***

7. Applicant did not traverse the examiner's statement that the effective filing date for all pending claims is 28 May 1999; thus the priority date is maintained for the reasons of record.

***Claim Rejections - 35 USC § 112***

8. Claims 42, 73, and 91 – 93 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated antibody sHlgM22 and fragments thereof which bind to oligodendrocytes *and* induce remyelination, does not reasonably provide enablement for monomers which do not bind oligodendrocytes, or for all recombinant antibodies derived from sHlgM22, or for antibodies or polypeptides comprising either SEQ ID NO:7 or 9 which do not bind oligodendrocytes, or for antibodies which bind oligodendrocytes but do not induce remyelination. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's amendment to claim 42 limits the scope of the claim somewhat. The claim now requires that the active fragments be capable of binding to oligodendrocytes. While sHlgM22 antibody does bind oligodendrocytes, this activity is not sufficient to impart the therapeutic function, namely inducing remyelination, to all antibodies that fall within the scope of

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claim 42. Claim 42 reads on fragments of antibodies, unlimited by size, which bind to oligodendrocytes. This activity, binding to oligodendrocytes, is not well-correlated with remyelination. In fact, the art indicates that administration of antibodies which bind to oligodendrocytes often result in demyelination. For example, Laughlin et al. (1997. *Journal of Neuroscience Research* 47:384-392) teach that antibodies raised against myelin oligodendrocyte glycoprotein (MOG) actually induce demyelination, rather than remyelination (see p. 388, second column). The specification does not teach the artisan how to use demyelinating antibodies. Claims 42 and 91 only require that the antibody or fragment bind to oligodendrocytes, and do not require that they induce remyelination or have any beneficial effect.

There is no requirement that the “monomers” be able to bind oligodendrocytes, and it is not immediately obvious what is encompassed by the term “monomer”. The term monomer is not explicitly defined in the specification, and it is not immediately obvious what distinguishes a monomer of the antibody from a monomeric amino acid. While Example 12 discloses the results of experiments on “monomers” made by reducing disulfide bonds, as the term is not explicitly defined in the specification and the monomers recited in claim 42 do not have to bind oligodendrocytes or have therapeutic utility, the claim reads on an unlimited number of possible monomers for which enablement has not been demonstrated and would not be expected to be useful. Similarly, the “recombinant antibodies derived” from sHIgM can be of any structure, or any function. As set forth in the paragraph spanning pp. 5 – 6 of the previous office action, no structure is required in the derivatives, and no function is required either. The claim thus reads on an unreasonable number of possible antibodies for which enablement has not been demonstrated.

Amended claim 73 and new claims 91 – 93 similarly do not require that the antibody or pharmaceutical composition be capable of binding to oligodendrocytes or be able to be effective in promoting remyelination. Antibodies are made of heavy and light chains, both of which are necessary for binding of the antigen, and these two chains work in a cooperative fashion to ensure complete binding. Claims 73 and 91 – 93 do not require that both the heavy and light chain variable regions be present, and those peptides that lack either of these regions would not be expected to bind or to have remyelinating activity. Alberts (1994. *Molecular Biology of the Cell*, pp. 1208 – 1220) teaches the structure of antibodies. Antibodies are comprised of two light chains and two heavy chains. The N-terminal regions of the light and heavy chains

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together form the antigen-binding region; see Figure 23-17 from Alberts, for example. If either the heavy or light chain is missing, the antigen-binding region is incomplete and the antibody will not be expected to bind to its cognate antigen. Thus claims which require only the presence of a single chain, such as new claims 91 – 93 are not fully enabled. Furthermore the breadth of these claims allows for the presence of other chains are also not fully enabled, for the same reason. Claim 92 allows for the antibody to include any light chain, whether or not that chain is capable of inducing remyelination either on its own or in conjunction with the heavy chain variable region set forth in SEQ ID NO:7. Claim 93 allows for the antibody to include any heavy chain, whether or not that chain is capable of inducing remyelination either on its own or in conjunction with the light chain variable region set forth in SEQ ID NO:9. As neither claim 92 or 93 requires that the antibodies be capable of inducing remyelination, and a substantial portion of the members falling within the scope of the claimed genera would not be expected to induce remyelination, the specification does not disclose to the artisan how to use the full scope of the invention recited in these claims. Similarly, claim 91 only requires the presence of either SEQ ID NO:7 or 9, but does not require the presence of both, and does not require that the claimed antibodies or active fragments thereof be capable of inducing remyelination. The specification does not disclose to the artisan how to use antibodies which bind to oligodendrocytes but do not induce remyelination.

With respect to claim 73, the same analysis also applies. There is no requirement that the pharmaceutical composition be able to induce remyelination. While the antibody sHlgM22 comprises both SEQ ID NO:7 and 9, the pharmaceutical composition of claim 73 does not; it is a pharmaceutical composition comprising either SEQ ID NO:7 or SEQ ID NO:9. The claimed composition does not include both these regions, and does not include the many other molecular regions which are parts of antibodies, such as the complete heavy and light chains and the hinge region (see Alberts, p. 1209). The specification does not teach the artisan how to use the pharmaceutical composition which consists of only SEQ ID NO:7 or 9 and a carrier, diluent, or vehicle. As explained in further detail above, Alberts teaches that both the light- and heavy-chain variable regions are necessary for an antibody to recognize its antigen but claim 73 does not require both regions, and does not require that the composition have any particular activity, such as the ability to induce remyelination.

Thus the rejection for lack of enablement commensurate in scope with the claims stands.

9. Claims 42 – 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for the reasons of record.

The examiner has determined that in order for a skilled artisan to make the claimed antibodies, the artisan must have access to the hybridoma that produces the antibodies. The specification does not provide sufficient assurance that all of the conditions of 37 CFR sections 1.801 through 1.809 have been met.

Applicant argues, on p. 7 of the remarks, that because certain exemplary sequences of the antibody sHIgM22 are described in the specification, access to the hybridoma is not necessary for one of skill in the art to make this antibody. The examiner disagrees. The claim reads not only on antigen-binding fragments such as the heavy- and light-chain regions variable regions, but reads on the entire antibody. The skilled artisan would be well aware that an antibody is a complex molecule made up of many different regions, many of which can vary. For example, see the enclosed text by Abbas (2005. Cellular and Molecular Immunology, Fifth Edition, Updated Edition, pp. 43 – 56). Abbas teaches that while antibodies all share certain general structures, there is variability between antibodies. For example, the heavy chains range in weight from 55 to 70 kD (see p. 48). The C (constant) regions are not involved in antigen binding, but mediate different effects of antibodies. The so-called “constant” regions actually can vary between antibodies (see pp. 51 – 53). Antibodies typically comprise a hinge region, but this region can vary in length from 10 to 60 amino acids (see p. 54). As claims 42 and 43 read on the intact sHIgM22 antibody, and there are so many regions which vary from one antibody to the next, it would not be possible for one of skill in the art to make this monoclonal antibody in the absence of the hybridoma that produces it. Thus the rejection for failing to have met all the requirements for deposit as set forth in paragraph 14 of the previous office action is maintained.

10. Claims 42 and 91 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

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relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

This rejection is maintained for the reasons of record and applied to the new and amended claims for the reasons explained below. Applicant argues, on p. 8 of the remarks, that the amendments to claim 42 are sufficient to overcome the rejection. However claim 42 still recites "monomers", which are not adequately described in the specification. The claim also recites "recombinant antibodies derived therefrom"; this term is not limited in either structure or function. No structure is required, no maximum number of changes permitted is specified in the claim, and there is no requirement that the recombinant antibody have a particular activity. Thus the claim reads on essentially any antibody which could be derived from the sHIgM22 antibody.

Applicant is directed to the flow chart on p. 9 of the Revised Written Description Interim Guidelines Training Materials, available on the internet at <http://www.uspto.gov/web/offices/pac/writtendesc.pdf>, which is analogous to the instant situation. Claim 42 is a genus claim, but neither the art nor the specification discloses a representative number of species falling within the genus. There is not even identification of any particular portion of the structure at either the nucleic acid or amino acid level that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Claims 42 and 91 each recite "active fragments thereof capable of binding oligodendrocytes". The specification discloses only a single member falling within this genus, namely sHIgM22. There is no disclosure of a genus of active fragments. Claim 91 allows for the inclusion of either the heavy- or light-chain variable regions of sHIgM22 in antibody, but the only disclosure in the specification is of antibodies comprising both regions, namely sHIgM22 itself. Claims 42 and 91 encompass very broad genera, but the specification only shows that applicant was in possession of a single member of the genus.

The instant disclosure of a single antibody, namely sHIgM22, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

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"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

While the quotations above from Fiers are on point to DNA, the same logic applies to antibodies as well. The specification does not describe the claimed invention in such detail so as to allow one of skill in the art to conclude that applicant invented the genus of antibody fragments which comprise SEQ ID NO:7 or 9 and bind to oligodendrocytes.

### ***Claim Rejections - 35 USC § 102***

11. Claim 42 is rejected under 35 U.S.C. 102(b) as being anticipated by PIR\_79 database accession number S05270, sequence last revised 30 June 1992.

Claim 42 encompasses "recombinant antibodies derived therefrom", referring to sHlgM22 and to "monomers thereof", which is a very broad limitation. The specification discloses that SEQ ID NO:9 is the light chain variable region of this antibody. As shown by the enclosed sequence alignment, S05270 is 95.6% identical to SEQ ID NO:9. The limitations "recombinant" is a product-by-process limitation, and only describes how a biological material is made. The term "derived therefrom" allows for considerable breadth as the term indicates that either the sHlgM22 antibody or one of its monomers, such as a single-chain of the antibody, could be used as a starting material. Given that the Ig lambda chain precursor molecule

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S05270 is very close in sequence to the instant SEQ ID NO:9, it can be derived from a monomer of sHlgM22 by changing and deleting certain amino acids from SEQ ID NO:9 and thus fairly anticipates the claimed invention.

**Conclusion**

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel E. Kolker, Ph.D.

May 5, 2006

  
JANET L. ANDRES  
SUPERVISORY PATENT EXAMINER